

Practitioner's Docket N . MBIO99-030CP1M

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Barnes, Thomas M., et al.
Application No.: 09/578,063 Group No.: 1646
Filed: May 24, 2000 Examiner: Dong Jiang
For: TANGO 294, A LIPASE-LIKE PROTEIN (formerly PROTEINS HAVING
DIAGNOSTIC, PREVENTIVE, THERAPEUTIC, AND OTHER USES)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION

Madam:

I, Paul J. Paglierani, hereby declare that:

1. I am the attorney of record in the above-identified patent application.

CERTIFICATION UNDER 37 C.F.R. SECTIONS 1.8(a) and 1.10*

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Practitioner's Docket N . MBIO99-030CP1M***PATENT***

2. Plasmids containing clone EpT294, encoding human TANGO 294 polypeptides described in the above-identified patent application, were deposited with the American Type Culture Collection (ATCC®), 10801 University Boulevard, Manassas, VA 20110-2209, on April 20, 1999 under the terms of the Budapest Treaty and assigned (composite) ATCC® Accession Number 207220.

3. Upon granting of a patent on the above-identified patent application, all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed.

I hereby declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issued thereon.

May 13, 2003

Respectfully submitted,

MILLENNIUM PHARMACEUTICALS, INC.

By _____

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by restricted, repetitive, and stereotyped patterns of behavior, interests, and activities often with above average performance in a narrow field against a general background of deficient functioning — called also *Asperger's disorder*
As-per-ger \ˈās-ˌpər-ˌgər/, flams, 20th century Austrian psychiatrist. Asperger first described the syndrome that bears his name in an article published in 1944.

as-per-gil-lin \as-pər-ˈjil-ən/ n 1: an amorphous black pigment found in the spores of various fungi of the genus *Aspergillus* 2: an antibacterial substance isolated from two molds of the genus *Aspergillus* (*A. flavus* and *A. fumigatus*) and reported to possess activity against both gram-positive and gram-negative bacteria

as-per-gil-lo-sis \as-pər-(ˈ)jil-ə-ˈd-sis/ n, pl -lo-ses \-sēz/ : infection with or disease caused (as in poultry) by molds of the genus *Aspergillus*

as-per-gil-lus \ˈjil-əs/ n 1 cap: a genus of ascomycetous fungi with branched radiate sporophores including many common molds 2 pl -gil-li \ˈjil-lī-, -(ˈ)l/ : any fungus of the genus *Aspergillus*

asper-ma-tism \ˈ(ˈ)ā-ˈspər-mə-ˈtiz-əm/ n: ASPERMIA

asper-mia \ˈspər-mē-ə/ n: inability to produce or ejaculate semen — compare AZOOSPERMIA — asper-mit \ˈmīk/ adj

asper-ic \ˈ(ˈ)ā-ˈsf(ə)-ik-, -ˈsfər- or asper-ical \-i-kəl/ adj: departing slightly from the spherical form esp. in order to correct for spherical aberration (an ~ lens)

as-phyx-ia \as-ˈfīk-sē-ə, -sē-ə/ n: a lack of oxygen or excess of carbon dioxide in the body that is usu. caused by interruption of breathing and that causes unconsciousness — compare SUFFOCATION — as-phyx-i-al \-sē-əl/ adj

as-phyx-i-ant \-sē-ən/ n: an agent (as a gas) capable of causing asphyxia

as-phyx-i-ate \-sē-āt/ vb -at-ed; -at-ing vt: to cause asphyxia in; also: to kill or make unconscious through inadequate oxygen, presence of noxious agents, or other obstruction to normal breathing ~ vi: to become asphyxiated — as-phyx-i-a-tion \-fīk-sē-ˈā-shən/ n — as-phyx-i-a-tor \-fīk-sē-āt-ər/ n

as-plid-i-nol \ə-ˈspīd-ˈn-ōl, -ōl/ n: a yellow crystalline compound C₁₂H₁₄O₄ found in the rhizome of the male fern

as-plid-i-um \as-ˈpīd-ē-əm, -sē-/ n, pl -ia \-ē-ə/ : a drug consisting of the rhizome and stipes esp. of the male fern used as the oleoresinous extract for the expulsion of tapeworms

as-pli-do-sper-ma \as-pə-(ˈ)dō-ˈspər-mə/ n 1 cap: a genus of tropical American trees or rarely shrubs of the dogbane family that includes the white quebracho 2: the dried bark of the quebracho (*Aspidosperma quebracho*) used as a respiratory sedative in dyspnea and in asthma — called also *quebracho bark*

as-pli-do-sper-mine \ˈspər-mēn, -mən/ n: a bitter crystalline alkaloid C₂₂H₂₉N₃O₂ that is obtained from quebracho bark and was formerly used in the form of its sulfate as a respiratory stimulant and antispasmodic and as an antipyretic in typhoid fever

as-pli-rate \ˈas-pə-ˈrāt/ vt -rat-ed; -rat-ing 1: to draw by suction 2: to remove (as blood) by aspiration (the portal vein is exposed and blood is aspirated with a 50-ml. syringe — *Biol. Abstracts*) 3: INHALE (aspirated material into the respiratory tract — *Anesthesia Digest*)

as-pli-rate \ˈas-p(ə)-ˈrēt/ n: material removed by aspiration

as-pli-ra-tion \ˈas-pə-ˈrā-shən/ n: a drawing of something in, out, up, or through by or as if by suction: as a: the act of breathing and esp. of breathing in b: the withdrawal of fluid or friable tissue from the body c: the taking of foreign matter into the lungs with the respiratory current — as-pli-ra-tion-al \-shənəl, -shən-əl/ adj

as-pli-ra-tor \ˈas-pə-ˈrāt-ər/ n: an apparatus for producing suction or moving or collecting materials by suction; esp: a hollow tubular instrument connected with a partial vacuum and used to remove fluid or tissue or foreign bodies from the body

as-pli-rin \ˈas-p(ə)-ˈrɔn/ n, pl aspirin or aspirins 1: a white crystalline derivative C₉H₈O₄ of salicylic acid used for relief of pain and fever 2: a tablet of aspirin

aspergillin • association 59

aspo-rog-e-nous \ˈ(ˈ)ā-spə-ˈrāj-ə-nəs, -spō- also aspo-ro-gen-ic \-spōr-ə-ˈjɛn-ik, -spōr- / adj: not spore-bearing; not producing spores (~ yeasts)

aspor-ous \ˈ(ˈ)ā-ˈspōr-əs, -ˈspōr- / adj: not having true spores

aspor-u-late \ˈ(ˈ)ā-ˈspōr-(y)ə-lət, -ˈspōr- / adj: not sporulating

as-sas-sin bug \ə-ˈsas-ˈn- / n: any bug of the family Reduviidae — compare CONENOSE

as-say \ˈas-ā, ə-ˈsā/ n 1: examination and determination as to characteristics (as weight, measure, or quality) 2: analysis (as of a drug) to determine the presence, absence, or quantity of one or more components — compare BIOASSAY 3: a substance to be assayed; also: the tabulated result of assaying

as-say \ə-ˈsā, ˈas-ā/ vt: to analyze (an impure substance or mixture) for one or more specific components (the sample was ~ed for drug content)

as-sim-i-la-ble \ə-ˈsīm-ə-lə-bəl/ adj: capable of being assimilated

as-sim-i-late \ə-ˈsīm-ə-lāt/ vb -lat-ed; -lat-ing vt 1: to take in and appropriate as nourishment; absorb into the system 2: to absorb into the cultural tradition of a population or group (the community assimilated many immigrants) ~ vi 1: to become absorbed or incorporated into the system (some foods ~ more readily than others) 2: to become culturally assimilated

as-sim-i-late \-lāt, -lāt/ n: something that is assimilated

as-sim-i-la-tion \ə-ˈsīm-ə-ˈlā-shən/ n 1 a: an act, process, or instance of assimilating b: the state of being assimilated 2: the incorporation or conversion of nutrients into protoplasm that in animals follows digestion and absorption and in higher plants involves both photosynthesis and root absorption 3: the process of receiving new facts or of responding to new situations in conformity with what is already available to consciousness — compare APPERCEPTION

as-sim-i-la-tive \ə-ˈsīm-ə-lāt-iv, -lāt- / adj: of, relating to, or causing assimilation

as-sim-i-la-to-ry \ə-ˈlā-tōr-ē, -tōr- / adj: ASSIMILATIVE

as-sist \ə-ˈsist/ vt: to give usu. supplementary support or aid to (~ the patient up the stairs) (~ respiration mechanically) ~ vi: to give support or aid

assist n: an act or procedure that provides assistance (external pressure circulatory ~ employs compression of the lower extremities — P. W. Wright)

as-sist-ed suicide \ə-ˈsist-əd- / n: suicide by a patient facilitated by means or information (as a drug prescription or indication of the lethal dosage) provided by a physician who is aware of how the patient intends to use such means or information

as-sn abbr association

as-so-ci-ate \ə-ˈsō-s(h)ē-āt/ vb -at-ed; -at-ing vt 1: to join or connect (things) together 2: to bring together in a relationship (infectious disease associated with a rise in body temperature) ~ vi 1: to combine or join with other parts (fibrils of the sensory neurons ~ with motor neurons — S. J. Jacob & C. A. Franccone) 2: to engage in free association (the patient associated freely about his childhood)

as-so-ci-ate \ə-ˈsō-s(h)ē-āt, -shət, -s(h)ē-āt/ adj: ranking immediately below the senior or chief position (~ clinical professor of medicine) (~ medical examiner)

as-so-ci-ate \ˈlīk/ n 1: a research worker or teacher affiliated with a professional organization or institution and ranking below a professor or full member (a research ~ in pathology) 2 often cap: a degree conferred esp. by a junior college (an Associate in Technical Arts degree in nursing — *Skagit Valley Coll. Catalog*)

as-so-ci-a-tion \ə-ˈsō-sē-ˈā-shən, -shē-/ n 1: the act of as-

about \ə-ˈbʊt/ kitten \ˈkɪtən/ further \ˈfʊrðər/ ash \ˈæʃ/ ace \ˈeɪs/ cot, cart \ˈkɒt/ out \ˈaʊt/ chin \ˈtʃɪn/ bet \ˈbet/ easy \ˈiːzi/ go \ˈgo/ hit \ˈhɪt/ ice \ˈaɪs/ job \ˈdʒɒb/ sing \ˈsɪŋ/ go \ˈgo/ law \ˈlɔː/ boy \ˈbɔɪ/ thin \ˈθɪn/ the \ˈði/ the \ˈði/ foot \ˈfʊt/ yet \ˈjet/ vision \ˈvɪʒən/ see also Pronunciation Symbols page

4 absorption accelerate

ab-sorp-tion \ab-'sɔrp-shən, -'zɔrp-\\ *n* 1: the process of absorbing or of being absorbed (of nourishment in the small intestine) — compare **ADSORPTION** 2: interception of radiant energy or sound waves

absorption coefficient *n*: the fraction of incident radiant energy which is absorbed per unit thickness, per unit mass, or per atom of an absorber — called also *coefficient of absorption*

absorption spectrum *n*: an electromagnetic spectrum in which a decrease in intensity of radiation at specific wavelengths or ranges of wavelengths characteristic of an absorbing substance (as chlorophyll) is manifested esp. as a pattern of dark lines or bands — compare **EMISSION SPECTRUM**

ab-sorp-tive \ab-'sɔrp-tiv, -'zɔrp-\\ *adj*: relating to or functioning in absorption (the ~ surface of the small intestine)

ab-sorp-tiv-ity \ab-'sɔrp-tiv-ə-tē, -'zɔrp-\\ *n*, *pl* -ties: the property of a body that determines the fraction of incident radiation absorbed by the body

ab-stain \ab-'stān, ab-\\ *vi*: to refrain deliberately and often with an effort of self-denial from an action or practice (as consumption of a food or a drug or indulgence in sexual intercourse) — **ab-stain-er** *n*

ab-ster-gent \ab-'stər-jənt, ab-\\ *adj*: having a cleansing or detergent effect

abstergent *n*: a substance used in cleansing; **DETERGENT**

ab-sti-nence \ab-'stə-nən(t)s\\ *n* 1: voluntary forbearance esp. from indulgence of an appetite or craving or from eating some foods 2: habitual abstaining from intoxicating beverages — **ab-sti-nent** \-nənt\\ *adj*

ab-tract \ab-'strakt\\ *n* 1: a written summary of the key points esp. of a scientific paper 2: a pharmaceutical preparation made by mixing a powdered solid extract of a vegetable substance with lactose in such proportions that one part of the final product represents two parts of the original drug from which the extract was made

ab-tract \ab-'strakt, ab-\\ *vt*: to make an abstract of — **ab-tract** *or* **ab-tract-er** \-tər\\ *n*

ab-t *abbr* about

abu-lia *or* **abou-lia** \ā-'b(y)ū-lē-ə, ā-\\ *n*: abnormal lack of ability to act or to make decisions that is characteristic of certain psychotic and neurotic conditions — **abu-lie** *also* **abou-lie** \-lik\\ *adj*

abuse \ā-'byūs\\ *n* 1: improper or excessive use or treatment (drug ~) — see **SUBSTANCE ABUSE** 2: physical maltreatment: as a: the act of violating sexually: **RAPE** b: under some statutes: rape or indecent assault not amounting to rape

abuse \ā-'byūs\\ *vt* abused; **abus-ing** 1: to put to a wrong or improper use (~ drugs) 2: to treat so as to injure or damage (~ a child) 3 a: **MASTURBATE** b: to subject to abuse and esp. to rape or indecent assault — **abus-able** \-b(y)ū-zə-bəl\\ *adj* — **abus-er** *n*

abut-ment \ā-'bət-mənt\\ *n*: a tooth to which a prosthetic appliance (as a denture) is attached for support

ac *abbr* 1 acute 2 [Latin *ante cibum*] before meals — used in writing prescriptions

Ac *symbol* actinium

AC *abbr* alternating current

aca-cia \ā-'kā-shə\\ *n* 1 *cap*: a genus of woody leguminous plants of warm regions having pinnate leaves and white or yellow flower clusters — see **CATECHU** 2: any of the genus *Acacia* of leguminous plants 3: **GUM ARABIC**

acal-cu-lia \ā-'kal-'kal-'kyū-lē-ə\\ *n*: lack or loss of the ability to perform simple arithmetic tasks

acal-cu-lous \ā-'kal-'kyā-ləs\\ *adj*: not affected with, caused by, or associated with gallstones (an ~ gallbladder) (~ cholecystitis)

acan-thi-on \ā-'kan(t)-thē-ən, -thē-ān\\ *n*: a point at the base of the anterior nasal spine

Acan-tho-ceph-a-la \ā-'kan(t)-thē-'sef-ə-lə\\ *n* *pl*: a group of elongated parasitic intestinal worms with a hooked proboscis: that as adults lack a digestive tract and absorb food through the body wall, and that are usu. classified as a sep-

arate phylum related to the phylum Platyhelminthes

acan-tho-ceph-a-lan \ā-'kan(t)-thē-'lan\\ *n*: any of the phylum Acanthocephala of unsegmented parasitic worms — called also *spiny-headed worm* — **acan-tho-ceph-alan** *adj*

Acan-tho-chei-lo-ne-ma \ā-'ki-lə-'nē-mə\\ *n*: a common genus of tropical filarial worms parasitic in humans and monkeys

acan-tho-cyte \ā-'kan(t)-thē-'sīt\\ *n*: an abnormal red blood cell characterized by variously shaped protoplasmic projections

acan-thoid \ā-'kan(t)-thōid\\ *adj*: shaped like a spine

ac-an-thol-y-sis \ak-'an-'thāl-ə-'sīs, ā-'kan-, āk-'an-\\ *n*, *pl* -y-ses \-ə-'sēz\\: atrophy of the stratum spinosum of the epidermis

ac-an-tho-ma \ā-'thē-mə\\ *n*, *pl* -mas \-məz\\ *or* -ma-ta \-mə-tə\\: a neoplasm originating in the skin and developing through excessive growth of skin cells esp. of the stratum spinosum

ac-an-tho-sis \ā-'thē-səs\\ *n*, *pl* -tho-ses \-sēz\\: a benign overgrowth of the stratum spinosum of the skin — **ac-an-tho-sis** \-thāt-ik\\ *adj*

acanthosis \ā-'grī-kans \-'nis-rə-'kanz, -'nī-grə-\\ *n*: a skin disease characterized by gray-black warty patches usu. situated in the axilla or groin or on elbows or knees and sometimes associated with cancer of abdominal viscera

acap-nia \ā-'kap-nē-ə, (')-ā-\\ *n*: a condition of carbon dioxide deficiency in blood and tissues — **acap-ni-al** \-əl\\ *adj*

Ac-a-pul-co gold \ak-'ə-pūl-(i)'kō-, āk-\\ *n*: marijuana grown in Mexico that is held to be very potent

acar-dius \ā-'kard-ē-əs\\ *n*: one of a pair of twin fetuses that is formed without a heart and that is usu. joined to the other fetus on which it depends for its circulation

acari *pl* of **ACARUS**

ac-a-ri-a-sis \ak-'ə-'rī-ə-'sīs\\ *n*, *pl* -a-ses \-sēz\\: infestation with or disease caused by mites — called also *acarinosi*

acar-i-cide \ā-'kar-ə-'sīd-\\ *adj*: having a lethal effect on mites (an ~ compound)

acar-i-cide \ā-'kar-ə-'sīd\\ *n*: a pesticide that kills mites and ticks

ac-a-rid \ak-'ə-rəd\\ *n*: any of the order Acarina of arachnids; esp. any of the family Acaridae of mites — **acarid** *adj*

Acar-i-dae \ā-'kar-ə-'dē-ə\\ *n* *pl*: a large and widely distributed family of mites that feed on organic substances (as preserved meats, hides, seeds, and grains) and are sometimes responsible for dermatitis in persons exposed to repeated contacts with infested products — see **GROCEA'S ITCH**

Ac-a-ri-da \ak-'ə-'rī-nə, -'rē-\\ *n* *pl*: a cosmopolitan and very large order of the class Arachnida comprising the mites and ticks most of which lack distinct demarcation into cephalothorax and abdomen and have no book lungs, many of which are parasites of plants, animals, or humans, and some of which are vectors of important diseases

ac-a-rine \ak-'ə-'rīn, -'rēn, -'ran\\ *adj*: of, relating to, or caused by mites or ticks (~ dermatitis) — **acarine** *n*

ac-a-ri-no-sis \ak-'ə-'rī-nō-'sīs\\ *n*, *pl* -no-ses \-sēz\\: **ACARINOSIS**

ac-a-ro-der-ma-ti-tis \ak-'ə-'(r)ō-dər-mə-'tīt-əs\\ *n*: dermatitis caused by mites

ac-a-rol-o-gy \ak-'ə-'rāl-ə-'jē-\\ *n*, *pl* -gies: a branch of zoology that is concerned with the study of mites and ticks — **ac-a-rol-o-gist** \-jəst\\ *n*

ac-a-ro-pho-bia \ak-'ə-'rō-'fō-bē-ə, -'rā-\\ *n* 1: an abnormal dread of skin infestation with small crawling organisms 2: a delusion that the skin is infested with small crawling organisms

ac-a-rus \ak-'ə-'rəs\\ *n* 1 *cap*: a genus of arachnids including a number of small mites and formerly including all mites and ticks 2 *pl* **ac-a-ri** \-rī-, -'rē-\\: **MITES**; esp. one of the genus *Acarus* or formerly included in this genus

acathisia *var* of **AKATHISIA**

acau-dal \ā-'kōd-'l\\ *or* **acau-date** \-'kō-'dāt\\ *adj*: having no tail

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5.3 ASSIMILATION OF LIPIDS BY THE BODY

5.3.1 Digestion. Before dietary fats can be taken up and used by the body, they must first be broken down into their component parts by a variety of digestive enzymes

The bulk of dietary fat is provided by the triacylglycerols, which must be extensively hydrolysed to their constituent fatty acids before they can be assimilated by the body.

In most adults the process of fat digestion is very efficient and the hydrolysis of triacylglycerols is accomplished almost entirely in the small intestine by a lipase secreted from the pancreas. At birth, the newborn animal has to adapt to the relatively high fat content of breast milk after relying mainly on glucose as an energy substrate in fetal life. It is presented with two major problems in fat digestion: the pancreatic secretion of lipase is rather low and the immature liver is unable to provide sufficient bile salts to solubilize the digested lipids. These problems are even more acute in the premature infant. Yet the newborn baby can digest fat, albeit less efficiently than the older child or adult. This is now attributed primarily to the activity of a lipase secreted from the serous glands of the tongue (lingual lipase) which is carried into the stomach where hydrolysis occurs, without the need for bile salts, at a pH of around 4.5-5.5. The secretion is probably stimulated both by the action of sucking and the presence of fat in the mouth, although the evidence for this was obtained from experiments with rats rather than human babies. The products are mainly 2-monoacylglycerols, diacylglycerols and non-esterified fatty acids, the latter being relatively richer in medium chain length fatty acids than the original acylglycerols. There is also evidence that a lipase present in human breast milk contributes to fat digestion in the newborn. It is interesting that the milk fat of most mammals is relatively rich in medium chain length fatty acids rather than the usual 16-20C compounds. The relative ease with which lipids containing medium chain fatty acids can be absorbed certainly helps lipid uptake in babies.

As the baby is weaned on to solid food, the major site of fat digestion is shifting from the stomach to the duodenum. The stomach still has a role to play since its churning action creates a coarse oil-in-water emulsion, stabilized by phospholipids. Also, proteolytic digestion in the stomach serves to release lipids from the food particles where they are generally associated with proteins as lipoprotein complexes. The fat emulsion that enters the intestine from the stomach is modified by mixing with bile and pancreatic juice. Bile supplies bile salts, which in man are mainly the glycine and taurine conjugates of tri- and di-hydroxycholic acids, formed from